

## Lyme disease: How reliable are serologic results?

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See also, [www.cmaj.ca/lookup/doi/10.1503/cmaj.141413](http://www.cmaj.ca/lookup/doi/10.1503/cmaj.141413)

**L**yme disease is a tick-transmitted bacterial infection that is well established in North America. It is uncommon in most areas of Canada, but its incidence and geographic range are increasing. The accurate diagnosis of Lyme disease is critical to ensure that those patients who truly have the condition are given appropriate antibiotics. Furthermore, an accurate diagnosis ensures patients with nonspecific symptoms are not mistakenly told that they have Lyme disease. In their recent practice article,<sup>1</sup> Andany and colleagues discuss a clinical scenario in which a Canadian man pursued testing for Lyme disease through a commercial laboratory in the United States. The test showed a positive result that was at odds with serologic testing conducted through a public health laboratory.<sup>1</sup>

This patient scenario illustrates for readers that American specialty laboratories should not be considered to provide a more sensitive assay for the diagnosis of Lyme disease than their public health counterparts. Recent research has documented a high rate of false-positive results with extremely poor positive predictive value in some specialty laboratories.<sup>2</sup> Mistakes in diagnosis can deprive patients of treatment specific to the true cause of their symptoms, and can result in prolonged therapy for a condition they do not have.

The methods for diagnosing *Borrelia burgdorferi* infection, the organism that causes Lyme disease, have been continuously improving since the microbe was first discovered in 1982.<sup>3</sup> The method involves the use of European *Borrelia* species and flagellar antigens in the screening serology to improve the sensitivity or negative predictive value, and confirmatory Western blotting assays to increase the specificity and positive predictive value of the test.<sup>4,5</sup> Some Lyme disease advocacy groups espouse that Centers for Disease Control and Prevention (CDC) criteria used for the serologic diagnosis of Lyme disease are inadequate, and they recommend alternative interpretive standards.<sup>6</sup> However, a recent study by Fallon and colleagues<sup>2</sup> formally evaluated how current testing algorithms work in two patient groups and several types of laboratories

in the US. The findings support previous conclusions of the CDC<sup>7</sup> and highlight two important lessons for physicians and consumers.

In a well-defined cohort of patients with post-treatment symptoms of Lyme disease, tests done in a university or commercial laboratory using well-defined CDC criteria for the serologic diagnosis of Lyme disease were as sensitive as testing done in laboratories specializing in Lyme testing. This remained true even when the specialty laboratories used in-house criteria to “increase” the sensitivity of their Western blot testing. Accordingly, such laboratories cannot be considered to be better at picking up infections missed by standard CDC criteria.

Furthermore, 40 patients without Lyme disease were included in the study as a negative control group. The inclusion of immunoglobulin M in the interpretation of control group Western blot samples led to false-positive results from three of the four laboratories studied (a rate of 2.5%–25%). One specialty laboratory using in-house criteria (immunoglobulins G or M) had false-positive results in 57% of the samples from the negative control group.

Fallon and colleagues’ study further dispels the myth that US specialty laboratories provide a more sensitive assay for the diagnosis of Lyme disease, and documents a high rate of false-positive results with poor positive predictive values in some specialty laboratories. As a conse-

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### KEY POINTS

- The serologic diagnosis of Lyme disease in Canada is best done using standard laboratory protocols as implemented by the National Microbiology Laboratory of Canada using criteria recommended by the Centers for Disease Control and Prevention.
- Recent evidence suggests that standard assays and testing algorithms used in Canada are as sensitive as those used in American specialty laboratories for detecting infection with *Borrelia burgdorferi*.
- Specialty laboratory tests have a high rate of false-positive results owing to their use of non-evidence based interpretation criteria, particularly when results rely solely on Western blot analysis.
- Most Canadians who are told that they have Lyme disease based solely on results from specialty laboratory typically have other causes for their symptoms.

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quence, patients and physicians should be cautious in choosing a referral laboratory in the US when seeking “second opinion” serology after receiving a negative test result in Canada. Laboratories that use the standard CDC two-tier testing algorithms should be preferred over those that report results based on unproven, unvalidated, in-house criteria. Any positive result from a test that relies solely on Western blotting is most likely a false-positive.

Patients with chronic subjective symptoms without a diagnosis can be vulnerable and desperate for an answer as to the cause of their illness. Giving them a false diagnosis based on flawed testing is misleading. Inappropriate therapy based on such results leads to economic, psychological and physical adverse outcomes.<sup>8-10</sup> Rather, these patients deserve a complete and accurate evaluation to detect illnesses for which appropriate interventions can be applied and, whatever their diagnosis, supports to improve the quality of life for themselves and their families.

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